PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 02-1270-A)

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| **In application of** | ) | |
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| ~~**J. Fruehauf, *et al.***~~ | ) | ~~**Examiner: Lei Yao**~~ |
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| **Serial No. 10/734,880** | ) | |
| | ) | **Group Art Unit: 1642** |
| **Filed: December 12, 2003** | ) | |
| | ) | |
| **For: Gene Related Sensitivity and Resistance To Chemotherapeutic Drug Treatment** | ) | **Confirmation No.: 1031** |

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-14501

**RULE 132 DECLARATION OF WILLIAM RICKETTS-**

**APPENDIX A**

# William A. Ricketts, Ph.D.

24 Mayapple Way
Irvine CA 92612
949-701-6361
wricketts1@cox.net

**OBJECTIVE**

Develop cancer diagnostics to determine the response of current drugs and companion diagnostics for new drugs that can improve the health and treatment of cancer patients.

**PROFESSIONAL EXPERIENCE**

**Oncotech Inc – Tustin, CA**

- **Vice President of Research and Chief Scientific Officer**, 2006 to present
  - Plan and manage all aspects of diagnostic development including screening, clinical validation, reimbursement, and technology review.
  - Support the sales force in selling our core clinical products to surgeons, medical oncologists, and gynecological oncologists.
  - Manage operations of our Pharmaceutical Services Division and support in sales of our services to the pharmaceutical industry.
  - Develop and maintain budgets for all four departments under my direction (Research, Clinical Research, Pharmaceutical Services, and Pharmaceutical Services Sales).
  - Represented our science, operations, and strategic advantages to the investment community.
  - Assisted in the acquisition of Oncotech by Exiqon A/S.
- **Director of Business Development**, 2005
  - Evaluated potential diagnostic tests for in-licensing to offer through our CLIA laboratory.
  - Managed operations for Pharmaceutical Services Division and support in sales of our services to the Pharmaceutical industry.
- **Pharmaceutical Services Study Director**, 2004
  - Planned and executed GLP studies in collaboration with our Pharmaceutical Services clients.
  - Wrote master service agreements, work statements, and final reports for our GLP studies.
  - Directly sold our services to the Pharmaceutical industry.

**Valeant Pharmaceuticals (formerly Ribapharm) – Costa Mesa, CA**

- **Project Leader**, 2000 - 2004
  - Identified new targets for anti-cancer therapies, validated their status as a target, and designed new cell based and in vitro screens.
  - Designed and validated assays for identifying protein kinase inhibitors as anti-cancer compounds.
  - Managed the anti-cancer high throughput screening effort in conjunction with Automation Biology and was responsible for the planning of all experiments to evaluate hits from HTS.

- Managed resources and integrated personnel to perform lead optimization on initial hits from primary cell based screen.
- Designed new compounds for testing in cell based and in vitro structure-activity studies.
- Managed resources and integrated personnel to perform lead optimization on initial hits from primary cell based screen.
- Completed mechanism of action studies and preliminary animal studies on an anti-cancer lead compound.
- Designed and established clinical trials protocols for an in-licensed Phase II compound.

**ISIS Pharmaceuticals – Carlsbad, CA**

- **Postdoctoral Fellow**, 1999 –2000
  - Identified potential new cancer drug targets by altering the expression of anti-apoptotic proteins with antisense technology to induce apoptosis in cancer cells and better understand the death signaling pathways.
  - Designed high throughput screening assays for the effects of oligonucleotides on apoptosis.

**University of California San Diego – La Jolla, CA**

- **Graduate Research Assistant**, Department of Endocrinology, 1994 - 1999
  - Demonstrated that the adaptor protein Shc can regulate signal transduction pathways through differential interactions with other signaling molecules.
  - Designed a series of point mutations in phosphorylation and protein-protein interaction sites to test the activity of Shc in different signaling pathways.
  - Designed, purified, and microinjected a series of recombinant proteins to ascertain the role of Shc in different signaling pathways.

**University of Virginia – Charlottesville, VA**

- **Laboratory Technician**, Department of Anatomy and Cell Biology, 1990 - 1994
  - Examined the role of protein phosphorylation at the chromosome kinetochore in chromosome movement and cell cycle checkpoint controls.
  - Developed several immunofluorescence labeling procedures to detect protein expression and phosphorylation on chromosomes.
  - Analyzed the potential role of gamma glutamyl transpeptidase in providing a growth advantage to cancer cells and tumors.
  - Optimized media conditions to determine if glutathione could be used by tumor cells to gain a growth advantage.

**University of Virginia – Charlottesville, VA**

- **Undergraduate Researcher**, Department of Microbiology, 1986-1990
  - Designed inducible mammalian expression vectors encoding mutant forms of c-src and assayed their effects on EGF signal transduction.

## OTHER PROFESSIONAL EXPERIENCE

**Membership in the American Association for Cancer Research**

**Regulatory Compliance for Biologics and Drugs Course**
UCSD Extension, *University of California, San Diego*
- An introductory course to FDA regulations and compliance.

**Service as a Reviewer**, Journal of Biological Chemistry

## EDUCATION

**University of California San Diego, Department of Biomedical Sciences – La Jolla, CA**
Doctorate of Philosophy, Biomedical Sciences (1999)

- Title of Dissertation: "The Roles of the Adaptor Protein Shc in Mitogenic Signaling"

**University of Virginia, Department of Biology**

- Bachelor of Arts, Biology (1990)

## PUBLICATIONS

d'Amato, T.A., Landreneau, R.L., **Ricketts, W.A.**, et al. *Survival among patients with platinum resistant, locally advanced non-small cell cancer treated with platinum-based systemic therapy.* Journal of Thoracic and Cardiovascular Surgery. In press.

d'Amato, T.A., Landreneau, R.L., **Ricketts, W.A.**, et al. *Chemotherapy Resistance and oncogene expression in non-small cell lung cancer.* Journal of Thoracic and Cardiovascular Surgery 133:352-363.

Sharma, P.M., Son, H., **Ricketts, W.A.**, and Olefsky, J.M. *Mechanism of SHIP mediated inhibition of Insulin and PDGF-stimulated MAP Kinase activity in 3T3-L1 adipocytes.* Molecular Endocrinology 19 (2): 421-30.

Ugi, S., Sharma, P.M., **Ricketts, W.A.,** Imamura, T., and Olefsky, J.M. *Phosphatidylinositol 3-kinase is required for insulin-stimulated tyrosine phosphorylation of Shc in 3T3-L1 adipocytes.* Journal of Biological Chemistry: 277(21): 18592-18597.

Ugi, S., Imamura, T., **Ricketts, W.A.**, and Olefsky, J.M.. *Protein Phosphatase 2A forms a molecular complex with Shc and regulates Shc tyrosine phosphorylation and mitogenic signaling.* Molecular and Cellular Biology 22(7):2375-2387.

Dalle, S.F., **Ricketts, W.A.**, Vollenweider, P., Imamura, T., and Olefsky, J.M. *Insulin and IGF-I signaling differ in the involvement of G protein signaling components.* Journal of Biological Chemistry 276(19): 15688-15695.

Bannerman, D.D., Tupper, J.C., **Ricketts, W.A.**, Bennett, F.C., Winn, R.K., and Harlan, J.M. *A Constitutive cytoprotective pathway protects endothelial cells from inflammatory mediator-induced apoptosis.* Journal of Biological Chemistry 276(18): 14924-14932.

Collins, L.R., **Ricketts, W.A.**, Yeh, L., and Cheresh, D. *Bifurcation of cell migratory and proliferative signaling by the adaptor protein Shc.* Journal of Cell Biology 147(7): 1561-1568.

**Ricketts, W.A.**, Brown, J.H., and Olefsky J.M. *Pertussis toxin sensitive and insensitive thrombin signaling to Shc and mitogenesis is mediated by different mechanisms.* Molecular Endocrinology 13(12): 1988-2001.

**Ricketts, W.A.**, Collins, L.R., Olefsky, J.M., and Brown, J.H. *The G12 coupled thrombin receptor stimulates mitogenesis through the Shc SH2 domain.* Oncogene 15(5): 595-600.

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**Ricketts, W.A.**, Rose, D.W., Shoelson, S., and Olefsky J.M. *Functional roles of the Shc phosphotyrosine binding and Src homology 2 domains in insulin and epidermal growth factor signaling.* Journal of Biological Chemistry 271(42): 26165-26169.

Hanigan, M.H., Brown, J.E., and **Ricketts, W.A.** *Gamma-glutamyl transpeptidase, a glutathionase, is present in some cell culture grade bovine sera.* In Vitro and Cellular Developmental Biology 29A(11): 831-833.

Gorbsky, G.J. and **Ricketts, W.A.** *Differential expression of a phosphoepitope at the kinetochores of moving chromosomes.* Journal of Cell Biology 122(6): 1311-1321.

Hanigan, M.H. and **Ricketts, W.A.** *Extracellular glutathione is a source of cysteine for cells that express gamma-glutamyl transpeptidase.* Biochemistry 32(24): 6302-6.

## POSTERS, PRESENTATIONS, AND INVITED TALKS

**Ricketts, W.A.** October 20th, 2008, San Diego, Ca. *A New Diagnostic Platform for Prediction of Drug Response Based on Tumor miRNA Profiles.* D2D IBC Meeting.

Teoh, D., Holloway, R.W., **Ricketts, W.A.**, et al. The Association of ERCC1 and Clinical Outcomes of Women with Advanced Ovarian Cancer. ASCO 2008: 5575.

Zakashanskey, K., Bradley, W.H., Rahaman, J., Dottino, P., and **Ricketts, W.A.** *Comparitive Genomic Hybridization Predicts Time to Recurrence in Primary Ovarian Cancer.* Proceedings of the Society of Gynecological Oncologists 2008.

Søkilde, R., Høiby, P.E., Smith, D.L., **Ricketts, W.A.**, Møller, S. and Litman, T.H. *A new diagnostic platform for prediction of drug response based on a tumor's miRNA profile.* AACR 48: LB-288.

Søkilde, R., Høiby, P.E., Nielsen, B.S., Møller, S., **Ricketts, W.A.**, and Litman, T.H. *Global microRNA profiling using novel miRCURY LNA™ microarrays enables identification of tumors of unknown primary origin.* Keystone Symposium: RNAi, MicroRNA, and Non-Coding RNA 2008.

Jinawath, N., **Ricketts, W.A.**, et al. *The role of NAC-1 in the development of Taxol resistant ovarian cancer.* AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics 2007.

Balasubramanian, S. **Ricketts, W.A.**, et al. *Activity of a novel HDAC inhibitor PCI-24781 in colorectal cancer: Discovery and validation of biomarkers of sensitivity and resistance.* AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics 2007.

Smith, D.L., van Waes, M., and **Ricketts, W.A.** *Correlating Signal Transduction Protein Kinase Levels, SNPs, and Drug Resistance in Human Melanoma*. AACR Proceedings 46: 925.

Covic, S., Smith, D.L., and **Ricketts, W.A.** *Detecting Altered Expression and Activation of Signaling Pathways in Cisplatin Resistant Ovarian Cancer.* AACR Proceedings 46: 1363.

Re, A. and **Ricketts, W.A.** *A 96-well Soft Agar Based Assay for Testing Cell Lines and Tumors for Drug Resistance*. AACR Proceedings 46: 1363.

Smith, D.L., Shahbahrami, B, Covic, S., and **Ricketts, W.A.** *Identification of Amplifications and Deletions in Taxol Resistant Ovarian Cancer.* Proceedings of the Society of Gynecological Oncologists. 2006.

Smith, D.L., van Waes, M, and **Ricketts, W.A.** *Optimization of protocols and screening of Topoisomerase II for SNPs that predict response to etoposide and doxorubicin.* AACR Proceedings 45: 4487.

Somberg, R., **Ricketts, W.A.**, Smith, D., and Bulliet, B. *A new universal luminescent kinase assay for HTS.* AACR Proceedings 44: 4579.

**Ricketts, W.A.** May 3rd, 2003, San Diego, Ca. *Developing a High Throughput Cell Based Kinase Assay.* SRI Protein Kinase Meeting.

**Ricketts, W.A.** Sept. 9th, 2002, Boston, Ma. *Screening a chemically diverse library with novel kinase assays.* IBC Protein Kinase Meeting.

**Ricketts, W.A.**, Vollenweider, P., Clodi, M., Imamura, T., and Olefsky, J.M. *Insulin and IGFI signaling differ in the involvement of G protein signaling components.* Diabetes 48 (S1): 1468.

Collins, L.R., **Ricketts, W.A.**, Klemke, R., Yeh, L., and Cheresh, D. *A role for the adaptor protein Shc in cell migration on the extracellular matrix.* Molecular Biology of the Cell 9(S1): 301a.

**Ricketts, W.A.** and Webster, N.J. *The 66 kDa Isoform of Shc is Involved in Insulin Signaling.* Diabetes 46(S1): 279A.

**Ricketts, W.A.** *The role of Shc in G protein coupled receptor signaling.* University of California, San Diego, Department of Pharmacology, La Jolla, CA. (1996)

**Ricketts, W.A.** *Signal Transduction through the adaptor protein Shc* University of Maryland, Baltimore Co., Department of Physiology, Baltimore, MD. (1996)

**Ricketts, W.A.** and Olefsky, J.O. *The phosphotyrosine interaction domains of Shc interact differently in signaling by receptor tyrosine kinase and G protein coupled receptors.* Hood College Oncogene Meeting. (1996)

Morris, A.J., Haruta, T., Martin, S.S., **Ricketts, W.A.**, Gustafson. T.A., Rose, D.W., and Olefsky, J.M. *Interaction between IRS1 and the insulin receptor is required for some but not all of insulin's intracellular effects.* Diabetes 45(S1): 45A.

**Ricketts, W.A.**, Rose, D.W., and Olefsky, J.M. *Differential Interactions of Shc phosphotyrosine binding domains in insulin and epidermal growth factor signaling.* Diabetes 45(S1): 182A.

**Ricketts, W.A.** and Gorbsky, G.J. *Binding of $p34^{cdc2}$ at the kinetochores of mammalian cells is cell cycle dependent and regulated by phosphorylation.* Molecular Biology of the Cell 4(S1): 118a.

Gorbsky, G.J. and **Ricketts, W.A.** *Differential phosphorylation of kinetochores in prometaphase: Possible roles in directing chromosome movement and the onset of anaphase.* Molecular Biology of the Cell 3(S1): 344a.

**PATENTS**

**Ricketts, W.A.**, and Smith, D.L. *Reagents and Methods for Predicting Drug Resistance (Doxil and Gemcitabine).* US Patent Application (provisional).

**Ricketts, W.A.**, and Smith, D.L. *Reagents and Methods for Predicting Drug Resistance (Platinums).* US Patent Application (provisional).

Kerfoot, C., **Ricketts, W.A.**, and Smith, D.L. *Reagents and Methods for Predicting Drug Resistance (Taxanes).* US Patent Application 20060160114.

Zhang, W., **Ricketts, W.A.**, An, H., and Hong, Z. *Heterocyclic compounds and uses thereof.* US Patent Application 20060205026.

**Ricketts, W.A.**, Diaz, P. and Hong, Z. *Parallel Inducible Cell-Based Kinase Screen.* US Patent Application 20040039037.

Ackermann, E.J., Bennett, C.F., Watt, A.T., **Ricketts, W.A.**, and Dean, N.M. *Antisense modulation of c-FLIP expression.* US Patent Application 20040254137.